
Stem Cell Gene Therapy for HIV in AIDS Lymphoma Patients

Grant Award Details

Stem Cell Gene Therapy for HIV in AIDS Lymphoma Patients

Grant Type: Disease Team Therapy Planning I

Grant Number: DR2-05327

Investigator:

Name: Mehrdad Abedi

Institution: University of California, Davis

Type: PI

Disease Focus: Blood Cancer, Cancer, HIV/AIDS

Award Value: \$66,880

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: NCE

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Grant Application Details

Application Title: RUNNING TITLE: Stem Cell Gene Therapy for HIV in AIDS Lymphoma Patients

Public Abstract:

The Human Immunodeficiency Virus (HIV) is still a major health problem. In both developed and underdeveloped nations, millions of people are infected with this virus. HIV infects cells of the immune system, becomes part of the cell's genetic information, stays there for the rest of the life of these cells, and uses these cells as a factory to make more HIV. In this process, the immune cells get destroyed. Soon a condition called AIDS, the Acquired Immunodeficiency Syndrome sets in where the immune system cannot fight common infections. If left untreated, death from severe infections occurs within 8 to 10 years. Although advances in treatment using small molecule drugs have extended the life span of HIV infected individuals, neither a cure for HIV infection nor a well working vaccine could be developed. Drug treatment is currently the only option to keep HIV infected individuals alive. Patients have to take a combination of drugs daily and reliably for the rest of their lives. If not taken regularly, HIV becomes resistant to the drugs and continues to destroy immune cells. What makes this situation even more complicated is the fact that many patients cannot take these drugs due to severe side effects.

Stem cell gene therapy for HIV may offer an alternative treatment. Blood forming stem cells, also called bone marrow stem cells make all blood cells of the body, including immune system cells such as T cells and macrophages that HIV destroys. If "anti-HIV genes" were inserted into the genetic information of bone marrow stem cells, these genes would be passed on to all new immune cells and make them resistant to HIV. Anti-HIV gene containing immune cells can now multiply in the presence of HIV and fight the virus. In previous and current stem cell gene therapy clinical trials for HIV, only one anti-HIV gene has been used. Our approach, however, will use a combination of three anti-HIV genes which are much more potent. They will not only prevent HIV from entering an immune cell but will also prevent HIV from mutating, since it would have to escape the anti-HIV effect of three genes, similar to triple combination anti-HIV drug therapy. To demonstrate safety and effectiveness of our treatment, we will perform a clinical trial in HIV lymphoma patients. In such patients, the destruction of the immune system by HIV led to the development of a cancer of the lymph nodes called B cell lymphoma. High dose chemotherapy together with the transplantation of the patient's own bone marrow stem cells cures B cell lymphoma. We will insert anti-HIV genes in the patient's bone marrow stem cells and then transplant these gene containing cells into the HIV infected lymphoma patient. The gene containing bone marrow stem cells will produce a new immune system and newly arising immune cells will be resistant to HIV. In this case, we have not only cured the patient's cancer but have also given the patient an HIV resistant immune system which will be able to fight HIV.

Statement of Benefit to California:

As of September 30, 2010, over 198,883 cumulative HIV/AIDS cases were reported in California. Another 40,000 un-named cases of HIV were also reported before 2006 although some of them may be duplicates of the named HIV cases. Patients living with HIV/AIDS totaled 108,986 at the end of September 2010. These numbers continue to grow since new cases of HIV and AIDS are being reported on a daily basis and patients now live much longer. In fact, after New York, California has the second highest number of HIV cases in the nation. Although the current and improved anti-retroviral small molecule drugs have prolonged the life of these patients, they still have to deal with the emotional, financial, and medical consequences of this disease. The fear of side effects and the potential generation of drug resistant strains of HIV is a constant struggle that these patients have to live with for the rest of their lives. Furthermore, not every patient with HIV responds to treatment and not every complication of HIV dissipates upon starting a drug regimen. In fact, the risk of some AIDS-related cancers still remains high despite the ongoing drug therapy. Additionally, in the current economic crisis, the financial burden of the long term treatment of these patients on California taxpayers is even more obvious. In 2006, the lifetime cost of taking care of an HIV patient was calculated to be about \$618,900. Most of this was related to the medication cost. With the introduction of new HIV medications that have a substantially higher price and with the increase in the survival of HIV/AIDS patients, the cost of taking care of these patients can be estimated to be very high.

The proposed budget cuts and projected shortfall in the California AIDS assistant programs such as ADAP will make the situation worse and could result in catastrophic consequences for patients who desperately need this kind of support. Consequently, improved therapeutic approaches and the focus on developing a cure for HIV infected patients are issues of great importance to the people of California.

Our proposed anti-HIV stem cell gene therapy strategy comprises the modification of autologous hematopoietic blood forming stem cells with a triple combination of potent anti-HIV genes delivered by a single lentiviral vector construct. This approach would engineer a patient's immune cells in a way to make them completely resistant to HIV infection. By transplanting these anti-HIV gene expressing stem cells back into an HIV infected patient, the ability of HIV to further replicate and ravage the patient's immune system would be diminished. The prospect of such a stem cell based therapy which may require only a single treatment to cure an HIV infected patient and which would last for the life of the individual would be especially compelling to the HIV community and the people of California.

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